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REPORT ON WORK, ACHIEVEMENTS IN FIELD OF GENETICS

Achievements in Medical Genetics

Sofia SUVREMENNA MEDITSINA in Bulgarian No 6, 1982 pp 342-346

[Article by M. Tsoneva and Br. Ts. Bratanov. Paper submitted at the First National Congress on Medical Biology and Genetics, 13-15 November 1981]

[Text] During the 5 years since the second national conference on medical biology and genetics, which was held in 1976, scientific research in the field of medical genetics was expanded and intensified in Bulgaria.

The basic scientific studies conducted during that period were focused on the following:

- a. Determining the genetic status of the Bulgarian population;
- b. Establishing the clinical-genetic polymorphism of existing hereditary diseases;
- c. Studying environmental factors as possible mutagenic agents, inducing new chromosomal and hereditary pathology.

The studies of the genetic status of the Bulgarian population cover both the nature and frequency of normal genetic human markers and the various hereditary and chromosomal pathology.

Fruitful and extensive studies were made on the characteristics and frequency of leucocytic antigena in our population, by a collective headed by Dr Minev. In addition to their theoretical value, these studies are directly related to clinical and practical health care problems.

The rapidly developing knowledge in the field of genetic polymorphism of enzymes, sera and other antigena and protein fractions has been the reason for extensive population studies of the dissemination of such genetic markers in the Bulgarian population and a contribution to its anthropological characterization.

Studies were made of genetic polymorphism and frequency of polymorphic alleles of phosphoglucosmutase (Pgm₁) (Kalchev), glyoxalase₁ (Popova), adenosine deaminase (Nenkov), esterase D (Rupcheva and Peev), post-transferrins (Pavlov), two aminotransferases, three oxyreductases and aldolase (Yaneva), the alpha₁-antitrypsine fraction (Tsoneva, Toncheva et al.), and others.

The dermatoglyphic studies of healthy individuals in our population (Karev), Duffy alleles (a, b, amorphen) and the secretion type in populations in various parts of the country (Tsoneva, Ilieva et al.) were contributions to the study of the normal genetic status of our population.

Problems of genetic polymorphism were developed on the chromosome level as well. Original studies include those on chromosome polymorphism (RV, C, Ag) in the Bulgarian population and its characteristic features in the various age groups (Tsoneva, Krachunova and Tsancheva).

Let us also emphasize the original studies made by G. Manolov and Ya. Manolova on improving the possibility of identifying human chromosomes through the use of prometaphasic chromosomes to this effect. This method enables us to determine a larger number of the ribbon differentiation of chromosomes and increases opportunities for chromosome diagnosis.

This period was characterized by extensive population studies of chromosome diseases in our country, hereditary degenerative diseases, some blood diseases (hemoglobinophies, G6 PD insufficiency, and hemophilia), some mental diseases, mucoviscidosis, phenylketonuria and galactosemia, hereditary blindness, hereditary deafness, Balkan endemic nephropathy, essential hypertension and ischemia, sugar diabetes and others.

Physicians-geneticists, pediatricists, neurologists, psychiatrists, internists, ophthalmologists, nose-ear-larynx specialists and others participated in the development of these broad genetic and clinical problems. This is a pleasing fact, for it indicates the direct penetration of genetics into clinical medicine, which leads to the rapid application of contemporary medical genetic achievements in practical health care.

It was established that 0.67 percent of newborn children suffer from chromosome diseases. Joint studies (Kushelov, Tsoneva et al.) conducted with Soviet scientists have indicated certain differences in the characteristics in chromosome pathology in our country. The Bulgarian population is characterized by a lower frequency of sex chromosome diseases and structural chromosome disturbances and a relatively higher incidence of trisomia 21.

Thirteen different chromosome defects, 5 of which are particularly rare, were discovered; among them partial trisomia 15q distale is a characteristic of a new chromosome syndrome. The nature of the mosaic forms and balanced translocations--which are important in the hereditary inheritance of chromosome diseases--was clarified.

Joint studies with Soviet researchers (Kuleshov, Tsoneva, Krachunova and Vulkova) determined that chromosome diseases account for 24.6 percent of all cases of inborn anomalies and degeneracies and 72 percent of stillborn cases.

The frequency of spontaneous mutations in the somatic cells of the population was determined: 0.94 percent, of which 0.84 percent are structural and 0.10 percent are number mutations.

In our overall assessment of cytogenetic studies conducted in our country, let us emphasize the original contributions of Manolov et al. in the cytogenesis of some malignant formations (Burkitt's lymphoma and leucoses). In Burkitt's lymphoma of the African and non-African types we see the systemic participation of chromosome 8, various fragments of which are translocated to individual chromosomes.

Comprehensive studies have been made of the incidence and nature of degenerative neurological diseases (Abadzhiev et al., Georgiev et al.), providing a complete population genetic characteristics of degenerative neurological diseases in Bulgaria. No such comprehensive studies have been made abroad. This is the first time in which neurological literature has described the incidence and gene frequency of autosome-recessive neural muscular atrophy, the AD and AR form of Schrumpel's disease, AR multiclonic epilepsy, myatrophic ataxia, and dyssynergia cerebellaris myoclonica (Hunt's disease).

From the clinical-genetic aspect, some interethnic characteristics of some inherited forms of progressive muscular dystrophies were identified. Clinical and biochemical criteria were applied to discover the carriers of X-recessive progressive muscular dystrophy (Yankov).

Comprehensive population-genetic studies (Krachunova et al., Milenkov et al.) of manic-depressive psychosis determined in 10 okrugs the frequency and genetic characteristics of the disease. This led to a determination of the frequency of bipolar and monopolar forms of the disease; the genetic heterogeneity of the psychosis was confirmed; for the first time the AR type of inheritance in monopolar manic-depressive psychosis (periodical depression) was determined.

Hemoglobinopathies and G6PD insufficiency are of particular interest in terms of our population.

Considerable contributions were made in the study of the incidence of hemoglobinopathies in our country during that period with the works of the Hematology Institute (Rashkov et al.), the Chair of Medical Genetics (Tsoneva, Mavrudieva, Toncheva, Lalchev), the Pediatrics Institute (Sh. Nin'o and Spasov), Cholakov at the Burgas Okrug Hospital, and others.

The studies indicated that there is a high incidence of hemoglobinopathies in our country. The incidence of thalassemias is particularly high (about 10 percent average heterozygotic carriers).

Among patients suffering from undetermined anemias 35.8 percent included hemoglobinopathies, 96.9 percent with a thalassemic syndrome and 3.1 percent with structural anomalies of the hemoglobin and mixed forms. These diseases are most widespread in southeastern Bulgaria and in our southern areas.

Descriptions were made of a variety of forms of thalassemias, including alpha-T (H), Leporet-Boston, Leporet-Washington, structural Hb mutations, O-Arabia, D-Punjab, Koln, etc. Particularly high, compared with other countries, is the incidence of O-Arabia Hb among our population.

These exceptionally valuable studies are of major theoretical importance in connection with the evolutionary factors which have shaped the genetic stock of the populations. They are also of great practical importance in terms of our health care.

The initial data on the incidence of hemophilia among children, obtained by the collective headed by Sh. Nin'o, are a contribution to the population-genetic studies of hematological hereditary diseases in our country. Along with the established gene frequencies and type of inheritance, the results of such studies are a valuable contribution to clinical polymorphism of hemophilia in Bulgaria.

Extensive population-genetic and clinical-genetic studies have been done on G6FD insufficiency in our population (Tsoneva, Mavrudieva, Toncheva, Lalchev).

These studies established the high frequency of G6FD insufficiency among our population: 4.1 percent hemihomo- and heterozygotic carriers among adults.

The high frequency of the defect among the newly born, compared with adults, was determined.

The genetic polymorphism of the G6FD gene was studied, in accordance with the WHO program. Thirteen different variants were identified, four of which were new. In the course of comprehensive studies with the collective of the Medical Genetics Institute in Moscow (Shchatskaya, Krasnopol'skaya) comparative studies were made of the G6FD variants in the Bulgarian, Russian and Azerbaijani populations, showing characteristic differences in the polymorphic nature of this genetic system, constituting a theoretical contribution to anthropogenetics.

Correlations of incidence of G6FD insufficiency with the altitude and endemic malaria in the past among our populations and with other genetic systems of the Th, Rh secretory type (Tsoneva et al.) have been established.

For the first time in our country we have established the role of G6FD insufficiency in the development of neonatal hyperbilirubinemia (Tsoneva, Novachev, Nacheva, Khatzhimekhedova et al.). About 20 percent of neonatal hyperbilirubinemia in our newborn is caused by G6FD insufficiency.

This theoretically and practically important problem in terms of our population (neonatal hyperbilirubinemia) was extensively studied by Novachev, who assessed the various genetic factors such as ABO and Rh incompatibility and G6FD insufficiency in the pathogenesis of neonatal hyperbilirubinemia in Bulgaria.

The role of G6FD insufficiency as a lethal and sublethal factor in our population was exposed. These extensive and systematic studies, which were summed up in the monograph "G6FD Nedostatuchnost v Bulgariya" [G6FD Insufficiency in Bulgaria] (M. Tsoneva, editor), are a theoretical contribution to the

anthropogenic characteristics of our population and are of direct health and social importance in all areas of our practical health care system.

During that period, mucoviscidosis, a hereditary disease which is not sufficiently appreciated in our country in terms of its comprehensive clinical importance, was the subject of population-genetic studies.

The gene frequency of mucoviscidosis was determined in some parts of the country and for the first time in the literature a description was provided of increased chromosome aberrations in the carriers of the mucoviscidosis gene, which is related to changed homeostasis in patients (Lukanov, Tsoneva, Radanova, Anadoliyska, Petkov and Andreeva). Data on the frequency of diabetes (Genkova, Tsvetkov) and of essential hypertonia (Tsonev, Kurnolski) in some parts of the country contribute to the population studies of hereditary diseases in the country.

Studies related to hereditary and congenital diseases, which lead to blindness in our population, carried out at the Institute for Eye Diseases (Dubov, Filipov) are of particular scientific value and significance in terms of health care. Hereditary factors play a role in 73.1 percent of the development of blindness in Bulgarian children. Such a study of the corresponding nosology and type of inheritance reveals valuable scientific facts of theoretical and important practical significance in the struggle against blindness in our country.

The laboratory for biochemical diagnosis of hereditary diseases, which was newly created under the Pediatrics Institute, undertook the implementation of a program for a mass screening for phenylketonuria and galactosemia, which will provide data on the frequency of these metabolic hereditary diseases among the population and will make it possible to undertake their treatment and prevention (Stanchev, Kalaydzhieva et al.).

During that period studies were made of the frequency and nature of congenital malformations in the various parts of the country: Pazardzhik (Kuyumdzhiev), Yambol (Karadimova), Ruse (Petrova), Sliven (Zhelyazcheva), Tolbukhin (Dzhenev and Georgieva) and others.

These studies indicated an increasing trend of congenital malformations in our country, a fact which is familiar on a worldwide scale, and which triggers justifiable concern.

Significant efforts are focused in scientific research on problems of clinical-genetic polymorphism of hereditary pathology and the role of genetic predisposition in pathological developments.

Systematic and profound studies are being made in this respect at the Ear, Nose and Throat Diseases Institute (Pavlov, Ficheva et al.) on hereditary audial pathology. These studies reveal the phenomenological characteristics of different nosological units such as mucopolysaccharidoses, osteogenesis imperfecta tarda, the Lawrence-Moon-Bidle, Uscher, Waardenburg and other syndromes in the development of hereditary deafness.

The type of heredity--AD, AR--was described and, using the most advanced audiometric methods, the intrafamily correlation and interfamily variability in the characteristics of audial disturbances were clarified.

Electron microscope studies of platella from the stirrup-bone (Pavlov, Tsenev, Ficheva, 1981) were a contribution to the clinical picture and pathogenesis of van der Hoeve's syndrome.

In addition to their theoretical values, these studies offered practical approaches for early audial rehabilitation and prostheses, which are particularly important in terms of the social adaptation of the deaf to society.

Comprehensive studies of the clinical-genetic polymorphism of G6PD insufficiency (Chair of Medical Genetics, Pediatrics Institute, Higher Medical Institute in Plovdiv and Pleven) proved the role of some genetic variants (Mediterranean, Corinthian, Seattle) in the development of specific pathologies--favism, neonatal hyperbilirubinemia, induced hemolytic reactions, chronic and acute hemolytic anemias, etc, affecting our population.

Noteworthy studies have been made of the role of some genetic markers in the development of a predisposition for diseases using multifactor etiology. They were carried out in terms of the HLA system, G6PD insufficiency, secretorial type, loss of taste, diabetes, thyrotoxicosis, schizophrenia, hypertonia, ulcers and others, conducted by various researchers (Minev, Genkova, Tsoneva et al., Kurnolski, Ilieva and others).

In this connection, dermatoglyphic studies must be considered genetic markers. They were carried out in the case of some eye diseases (Filipov, Stoykova), congenital heart diseases (Markova), some chromosome diseases (Kaleva) and others, which are of essentially theoretical significance and whose diagnostic value is insufficient.

Interesting studies were conducted during that period on the role of genetic factors in Balkan endemic nephropathy. Two independent groups (Mikhaylov and Markova and Boyadzhieva) proved AD-type heredity in this serious and mysterious disease existing in our country with convincing data. The results are rated highly. They offer a new strategy in our diagnostic and prophylactic approaches to the disease.

Other contributions to clinical genetics are the studies of hereditary lysosomic diseases and the large number of new diagnostic methods related to molecular diseases in our country, applied for the first time (Kalaydzhieva, Varon) are a contribution to clinical genetics. particularly useful in clinical cytogenetics were the use of bending techniques in some cytogenetic laboratories in Sofia--the Medical Genetics Chair (Georgieva, Tsancheva), the Oncological Institute (Manolov) and the Higher Medical Institute in Plovdiv (Vulkova, Genev). In this respect the monograph "Khromozomana Diagnostika" [Chromosome Diagnostics] (M. Tsoneva, editor) was useful. The introduction of the SCE (sister chromatoid exchanges) in the study of diseases related to chromosome instability (Georgieva) is an entirely new and promising direction in clinical genetics. In such studies, research on the level of SCE in man in different ontogenetic age groups (Tsoneva, Georgieva, Yulzari) is of particular theoretical and applied value (norming criteria).

This brief enumeration of studies and applications in the field of clinical genetics offers optimistic prospects regarding its future development. Medical genetics in our country is lagging behind our medical science and health care in only one essential aspect--the application and development of prenatal diagnosis, which is particularly necessary and valuable in the prevention of hereditary and chromosome pathology.

During the period under consideration, a large number of studies were made on problems of induced mutagenesis. Such studies combine the qualities of basic research and possibilities of direct practical application of results.

Problems of mutagenic characteristics of radiations were developed (Ivanov, Bayrakova, Vuglenov et al.), of possible protectors (antimutagens) in experiments and in individuals threatened with radiation, and others.

Direct studies were made of some biological factors such as toxins (Chan Thi Lien), viruses (Minchev) and autoimmune homeostasis (Krachunova). Extensive studies were made involving chemical mutagens, pesticides (Tsoneva, Georgieva, Dant Chi Than et al.), some medical compounds (Tsancheva, Georgieva, Ivanov), and industrial toxic substances such as vinylchloride, polyvinylchloride, styrene, and others. The SCE methods which were applied as a mutagenic test in the study of lymphocyte cultures in man (Tsoneva, Georgieva, Chan Thi Lien, Ivanov) as well as in vivo on animals (Syrian hamster and the cotton rat) were of particular value in enhancing the level of research in the field of induced mutagenesis.

Studies of professionally endangered groups of individuals in the chemical industry, which have led to the application of prophylactic measures whenever necessary, have been of particular value in the prevention of heredity and chromosomal diseases.

Studies of mutagenic characteristics of environmental factors in our country are included in the CEMA scientific program, and Bulgarian researchers are valued and respected partners in cooperative work on such problems.

The main directions which characterize these studies proved to be accurate and fruitful. They were included in the scientific coordination program "Genetic Status of the Bulgarian People and Factors Which Induce Mutations of the EMBF", which was set up in Bulgaria in 1980 in accordance with the CC of the BCP decrees on the development of medical science and cadres.

These directions must be consolidated and enriched through new nosological units. The diagnostic methods for the detection of hereditary and chromosomal diseases, particularly those involving prenatal diagnosis, must be improved.

A particularly important feature in the development of medical-genetic studies and the fast practical utilization of results are the organizational approaches adopted in their solution and, not least, the erudition of the scientific cadres.

These organizational approaches have been established--maximal integration of the cadre potential with specific scientific directions leading to the effective solution of the problems.

Medical-Genetic Consultation

Sofia SUVREMENNA MEDITSINA in Bulgarian No 6, 1982 pp 353-355

[Article by M. Tsoneva]

[Text] medical-genetic consultation (MGC) is a link within the health care system, whose task is to promote the prevention of hereditary and chromosome diseases.

In our country's health care system the MGC are controlled on the basis of the 1947 order of the minister of public health.

The MGC uses in its activities all achievements of general and medical genetics. Its activities are focused, on the one hand, on the family and the offspring and, on the other, the population.

Within the framework of the family, the MGC provides a genetic diagnosis of the respective disease which is the reason for the consultation and offers a prognosis on the risk of giving birth to a sick or damaged child in the respective family.

The MGC does not impose its decision on the family but provides advice regarding the actual dangers. The independent decision is made by the family in terms of the health and fate of its offspring. This form of medical-genetic consultation is defined as "passive" MGC, unlike activities aimed at the population, which are described as "active" MGC.

The active form of MGC is based on mass studies, screening programs, genetic monitoring, etc, organized and actively guided by the MGC.

The work of the MGC in limiting the birth of sick children suffering from hereditary and chromosome diseases has made extensive use of and contribution to prenatal diagnosis during the past decade.

With the help of prenatal diagnosis, which detects the chromosome or hereditary disease in the embryo, the possibilities of the MGC expanded. The birth of a healthy child became no longer a question of probability but of real possibility.

The problems of the MGC and prenatal diagnosis were the subject of a meeting of the First National Congress on Medical Biology and Genetics held in Bulgaria (13-15 November 1981). In addition to the papers submitted by Bulgarian authors, papers were submitted by a large number of foreign participants [all foreign names transliterated] such as Dr Machek, Prague; Dr Pelts, Rostok; Dr Weiss, Magdeburg; Lozanova and Tsinger, Berlin, GDR; Yokel, Gatersleden; and Metaxotou, Athens.

In terms of topics, the papers may be classified into three groups:

a. MGC and selective screening experience in our country (Tsoneva et al.; Khristozova et al.; Simeonov et al.).

- b. New methods and clinical approaches in diagnosing hereditary and chromosome diseases (Kremenski et al.; Lalov et al.; A. Kaleva).
- c. Experience and successes in prenatal diagnosis (Machek, Pelts et al.; Weiss et al.; Metaxotou et al.; Lozanova and Tsinger, Yokel).
- a. Between 1975 and 1980 more than 7,000 patients were subjected to MGC at the Chair of Medical Genetics in Sofia and 2,539 at the Higher Medical Institute in Plovdiv. The pathology subject to MGC was evaluated.

The highest frequency of reasons for MGC were chromosome diseases, degeneracies and congenital anomalies--35.32 percent, followed by reproduction failures (spontaneous abortions, stillborn)--18.13 percent. In terms of frequency they are followed by neurological diseases, 9.37 percent; hereditary blood diseases, 8.86 percent; mental diseases, 8.86 percent; internal diseases, 4.02 percent; metabolic, 2.16 percent; skin, 1.59 percent; eye, 1.24 percent; ear, 1.13 percent, and others (radiation damages, clinically unexplained cases, nonhereditary diseases), 5.25 percent.

A study of the sources of information which led the patients to MGC indicates that 48.09 percent of them were directed by a medical institution, no more than 7.28 percent by the polyclinics and 12.30 percent by medical personnel; 11.33 percent came on their own initiative and the source of information for 28.22 was not determined.

These data indicate the poor familiarity with the possibilities of MGC and their use on the part of medical workers in our polyclinics.

MGC would play a most important role in giving advice even before marriage in the case of individuals with hereditary pathology in order to prevent severe consequences to the family and society. The assessment of our experience on this level indicates that 98.56 percent of the consultations were postmarital and only 1.44 were premarital. The family seeks MGC at least after one misfortune. In 50 percent of the cases premarital consultations applied to mental illnesses, marriages between blood relatives, deafness, congenital luxation of the pelvic joint, i.e., diseases or situations which are quite clearly manifested in the family and society.

The application of the practical results of MGC in prenatal diagnosis is suffering from a considerable lag. Our initial successes in this respect were optimistic. In 1981 the first healthy child as a result of the application of prenatal diagnosis in the country was born. It was a case of a family with a single child with a severe hereditary chromosome disease, which was described for the first time in world literature (Tsancheva et al., 1981), with a high risk that other sick children would be born as a result of balanced translocation in the mother.

Our MGC includes genetic monitoring of professionally threatened groups from the effect of strong mutagenic agents and the use of preventive measures for the protection of gametogenesis and restricting a new outbreak of hereditary and chromosome pathology.

The range of the active form of MGC also includes studies of the role of genetic factors in mentally retarded children (Simeonov et al.) and selective screening for phenylketonuria and galactosemia (Kalaydzhieva et al.).

b. The second group of papers dealt with methodical problems of laboratory diagnosis of mucopolysaccharidoses and mucopolipidoses, clinical criteria in directing the patients to chromosome diagnosis, and the possibility of dermatoglyphics in diagnosing chromosome pathology.

c. Particularly rich and varied data were submitted based on the experience in the application of prenatal diagnosis in countries such as the GDR, Czechoslovakia and Greece.

Dr Machek from Prague reported on the results of prenatal diagnosis in Czechoslovakia, which covered about 2,000 cases. It has been applied since 1971. The main group (70 percent) of cases with prenatal diagnosis were based on indications of chromosome disease; 18.4 percent on defects in the neural tube, 3.8 percent of metabolic hereditary diseases, individual cases of mucoviscidosis, radiation risks, and others.

Docent Weiss shared the experience of his group based on 1,020 prenatal diagnoses made in Magdeburg. As a result of the data in 5.4 percent the pregnancy was interrupted as a result of the establishment of hereditary and chromosome diseases in the embryo. In real terms, this meant the prevention of the birth of 54 abnormal children.

Dr Pelts shared the experience of a group working in prenatal diagnosis in the city of Rostok in the GDR. This group includes gynecologists, geneticists, biologists and chemists. Dr Pelts emphasized that prenatal diagnosis is an interdisciplinary area which requires the joint efforts of specialists in different fields. In Rostok prenatal diagnosis has been applied since 1975 and the experience of the group is based on 282 pregnancies submitted to prenatal diagnosis. The characteristic feature of their approach in indications of prenatal diagnosis is to include in the risk group not only the mothers but the fathers, requiring the prenatal diagnosis in advanced age. The main group of prenatal diagnoses are based on indications of actual risk of the birth of a child with chromosome disease in more than 70 percent of the cases. In terms of incidence, this was followed by defects in the nervous tube--16 percent; congenital metabolic errors--1.4 percent, etc.

Lozanova and Tsinger reported on the results of 192 prenatal diagnoses in Berlin, GDR.

Dr Metaxotou et al. reported on 460 prenatal diagnoses in Athens. Prenatal diagnosis has been practiced in Greece since 1976.

The rapid popularity gained by prenatal diagnosis among society was stressed: it was practiced on six families in 1976, 142 in 1980 and 155 in the first 7 months of 1981 alone.

The main group of pregnancies with prenatal diagnosis was based on indications of the danger of chromosome diseases. In 4.7 percent of the prenatal diagnoses of pregnant women of an advanced age embryos with chromosome disease were diagnosed. In the course of the debates Dr Metaxotou pointed out that prenatal diagnosis of hemoglobinopathies is extensively applied in Greece, as they have a high incidence among the population. In this area of prenatal diagnosis another group is successfully working and is enjoying great popularity among the people.

The report by Yokel, from the Genetics Institute of the GDR Academy of Science in Gatersleden was of great interest.

He submitted preliminary results of his studies on prenatal diagnosis and the discovery of heterozygotic carriers of mucoviscidosis. This problem is exceptionally topical. Mucoviscidosis is a widespread hereditary disease among European populations and is the reason for a considerable rate of mortality in neonatal and early childhood. The study is focused on five lysosomic enzymes and alkalai phosphatase, which have been studied in terms of their specific activeness and some physical and chemical properties in cultures of skin fibroblasts in suspected individuals.

The results obtained are very encouraging and earmark possibilities of applying prenatal diagnosis in mucoviscidosis, which is of great health, social and economic significance.

In the course of the session a number of discussions took place on a high scientific level. They indicated the seriousness of the problems of MGC and prenatal diagnosis and their significance in terms of practical health care. Through MGC and prenatal diagnosis successes in medical genetics find a real application and yield results in the reduction of infant mortality, and the prevention of the birth of heavily damaged and defective children afflicting the family and society. In addition to its health and social aspect, this problem involves major moral and ethical aspects which must be emphasized.

The MGC and prenatal diagnosis problems which were raised and discussed at the First National Congress on Medical Biology and Genetics contributed to the clarification of these problems among our medical society and are a contribution to the extensive application of the contemporary successes in medical genetics in our practical health care.

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FLEXIBLE WORK CELL FOR MACHINING OF PRISMATIC WORKPIECES DESCRIBED

Bern TECHNISCHE RUNDSCHAU in German Vol 74 No 17, 27 Apr 82 pp 17, 19

[Article by U. Franz, engineer, VEB Fritz Heckert Machine Tool Combine, UDR 9039, Karl-Marx-Stadt: "Flexible Work Cell for the Complete Machining of Prismatic Workpieces--Minimum Attendance Operation With Integrated Measuring Functions"]

[Text] For the complete processing of prismatic small parts up to an edge length of 400 mm there has been developed a flexible manufacturing cell which is new and unconventional in its construction and mode of operation. Basically it is capable of functioning with few operating personnel to produce workpieces of stable quality. To this end measurement pickup devices are used in addition to thermal and optical surveillance equipment. The reduction of operating personnel is a consequence of the basic design of the machine and of the automation of hitherto neglected auxiliary functions. The design simultaneously solves problems involved in new configuration of workplaces and environmental problems. This system is advantageously influenced by harmonizing the machine with a new method of guidance.

It has been possible for both users and manufacturers to gather extensive experience from the use hitherto of processing centers. These form an important foundation for meeting demands for further development of new manufacturing facilities. Of elementary importance is the requirement for a process-optimal configuration, particularly in the domain of hitherto neglected auxiliary functions, for example, that of process lubrication and process cooling or the elimination of waste material from the work area. These questions are directly related to the minimization of operating and maintenance cost as well as to maximum protection of the operator from workroom dangers or from flying metal shavings and sprayed coolant.

There is a further important demand: namely, for the achievement of working accuracy not only under favorable conditions involving well-defined thermal machine conditions but also with high manufacturing stability at the highest possible statistical reliability of the required IT class in fully automatic operation and without continuous regulatory intervention on the part of the operator.

These requirements must also include the automatic establishment of prerequisite conditions for attaining work quality by means of measurement and quality control facilities as well as other appropriate measures.

These requirements can be met only with difficulty and by means of complicated devices when one is employing the conventional structures of processing centers. Therefore in designing the manufacturing cell presented here entirely new paths were opened up.

The development of guidance technology, especially its miniaturization, and the design maturity of decisive automating structural groups created the prerequisites for a "compact construction" which departs from the hitherto conventional individual setup of functional construction groups and methods of guidance and combines all of these into a "monoblock" occupying a minimal setup area.

A Broad Working Domain Is Included

Extensive investigations of the partial spectrum of the metal processing industry have shown that a large fraction of all prismatic parts including both edge parts and shaped parts may be included within a cube having an edge dimension of 400 mm. With axial paths of 480 mm it is possible for this cube to be reached from all sides by a tool having a diameter of 80 mm. The most important data for the flexible manufacturing cell are listed in Table 1. In part it may be inferred from this table that it is possible to perform economically all milling, boring, threading, countersinking and boring out operations with the tools used for these purposes today. The working material processed ranges over cast iron, steel, light metal and metal alloys as well as plastics.

Table 1. Most Important Technical Data for the Manufacturing Cell FCP 250

Chuckling area (palette)	mm	400 x 500
Displacement paths x, y, z	mm	480 x 480 x 480
Workpiece weight	N	1,500
Spindle cone	SK	45
Rpm range	min ⁻¹	20 to 4,500
Maximum driving power	kw	13.5
Maximum turning moment	Nm	440
Speed, fast forward	m/min	15
Automatically changeable tools	Number	40
Approximate area requirement	m ²	18

Construction and Function Are Simple and Practical

The exterior shape of the manufacturing cell FCP 250 is shown in Figure 1. Figure 2 explains the main construction of the actual work unit, especially with regard to the distribution and arrangement of the axes.

The workpieces are chucked on palettes at the chucking and tilting station (Figure 3) located at the right-hand frontal side. This is accomplished with

the receiving area being in a horizontal position. The chucking elements and devices are fastened by means of a cross-slot system.



Figure 1. Overall view of the FCP 250 manufacturing cell (Wema Auerbach, GDR).

After the chucking process has been completed by the operator the workpiece carrier tilts into a vertical position. After that there opens up the palette lock through which the workpiece carrier is brought into the rear portion of the workspace onto the side of a double-armed palette changer which is turned to face the transfer position of the processing station (Figure 4).

While the other receiving arm of the palette changer remains free in expectation of the return motion of the processed workpiece the temperature of the readied workpiece is brought to the processing temperature (preheated) by spraying it with a coolant which has been warmed by the process.

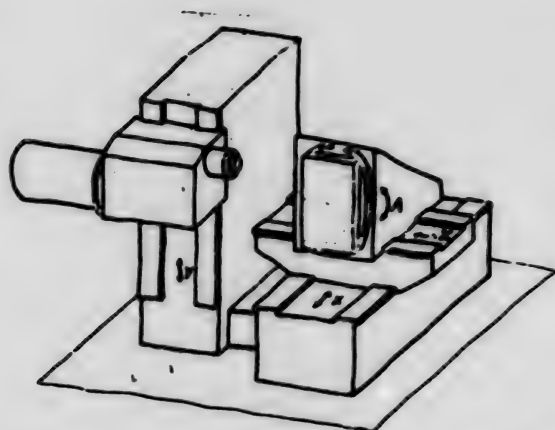


Figure 2. Construction of the basic machine FCP 250; distribution of the axes.

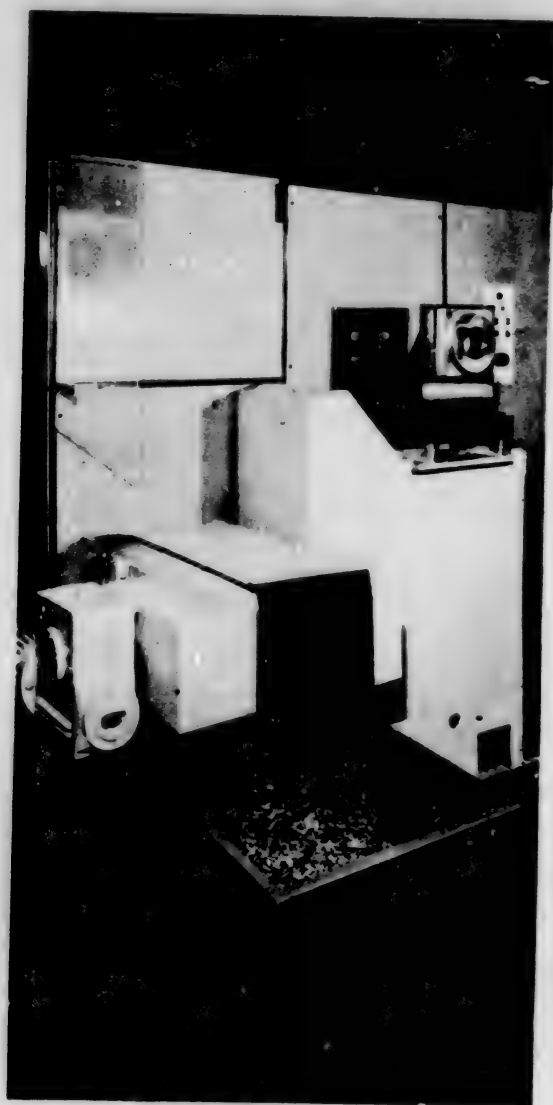


Figure 3. Chucking and tilting station.



Figure 4. View into the workspace in the direction of the workpiece flow. In the foreground the palette changer; behind that the working spindle and tool-changing arm.

After the program-processing and after moving into the changing position of the sled system a transport facility pulls the finished workpiece with its palette onto the changer. A 180° turn about a horizontal axis and the subsequent shift of the new palette onto the machine-side reception characterize the automatic changing process. While the new workpiece is being processed the one which has been worked is moved in the opposite direction back to the chucking site and can be replaced independently of the latter.

For the processing it is possible to use the flexibly storage-location coded work tools in arbitrary sequence. Four cooling nozzles arranged in circular symmetry and distributed over a conical region centered on the midline of the main spindle are adjustable and guarantee a cooling and lubricating effect adaptable to the greatest lengths of the tools (Figure 5).

This effect can be further differentiated by two pressure stages. Metal shavings are in this way simultaneously removed over the most rapid and direct path from the workpiece and from its supporting and moving structural components; these metal shavings drop together with the used coolant into the metal shaving transporter which is located directly under the work site. Here the coolant is separated out when it trickles into a container lying below.

From there when necessary it passes via an externally placed moving belt filtering automatic apparatus into a cooling device situated above in order that it may continue to circulate at a constantly low temperature. In order to

avoid muddy deposits in the coolant chamber the medium is whirled through spray nozzles and transported to the outside via the pumping system together with the general circulation.



Figure 5. Work spindle head together with program-adjustable coolant nozzles built into the frontal side of the sledge.

Consistently with the requirements that powerfully injected and large coolant volumes must be kept under control the workspace is fully encapsulated (Figure 6) with fixed and movable protective equipment. Openings, for the most part closable, are present only for automatic workpiece changing or tool changing, for the intervention of the double-armed changer and for the removal of shavings in the area of the transporter. In this way with the help of a ventilator there is obtained in the interior a stable microclimate to secure small temperature differences for a workpiece precision which is uniformly high and which depends little upon time.

Working along these lines are temperature sensors attached to the support which signalize the presence of a uniform support position such as required for precision processing.

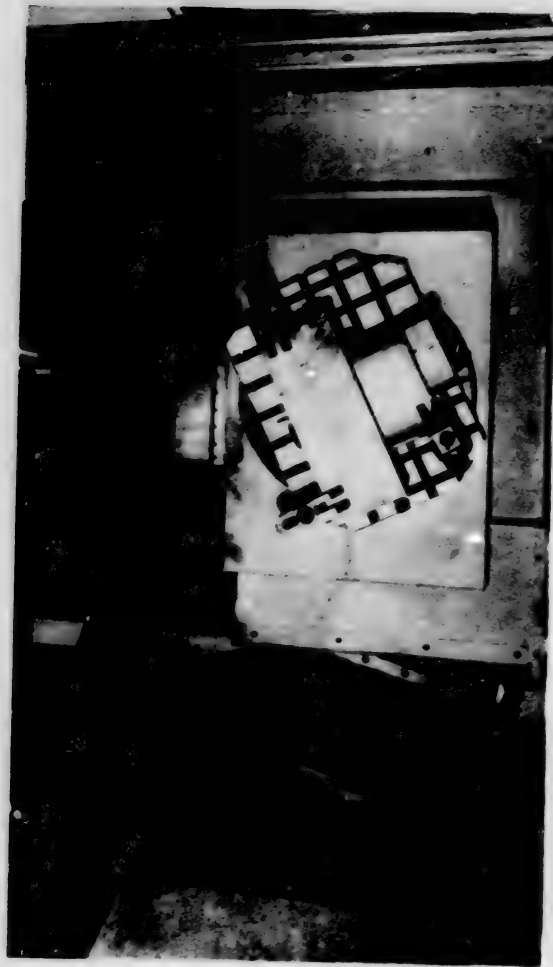


Figure 6. View into the fully encapsulated workspace. In the background the pallet with workpiece chucked in place together with the working spindle and above left the tool-changing arm.

The principal drive is to a special degree designed for thermal constancy. In this two routes are followed. The first places emphasis on the requirement that but little heat is produced in the entire functional unit. The second requires that the nevertheless unavoidable heat shall be removed as rapidly as possible before it can have any effect upon the sledge components and supporting structure components which are subject to possible damage as a result of shifted position.

These measures start with the selection of the proper spindle bearings. For this one employs permanently lubricated radial-oblique ball bearings. Intensive heat sources in the form of electromagnetically switched couplings and brakes are avoided.

Hydraulically actuated linear gear-tooth couplings link the two transmission ranges with the lower rpm range being transmitted via a spur gear stage and the upper via a toothed belt drive. Thus there results a low number of heat-generating bearings, i.e., meshing gears or belts.

An intensive oil circulation serves to eliminate the resulting heat. Fresh oil first bathes the bearings of the main spindle and then runs over the walls of the housing, the meshing gears and the bearings. The former possess a white reflective coating of lacquer so that the heat is not absorbed but is radiated off into the cooling oil (thermos bottle effect).

Guiding Devices and Path-Measuring Principle Perform Important Tasks

The requirement of high workpiece accuracy is met moreover by the design of the guiding devices and the choice of the path-measuring principle employed. The guiding devices have in addition the task of providing good damping of an efficient cutting process in which a turning moment of 500 Nm can be transformed into cutting forces. They are therefore designed as a combination of sliding and rolling guides. The applied forces are reacted by stick-slip-free cast plastic guides coupled with steel or gray cast iron. The narrow guides and the directional guides are gripped with zero-play by peripheral roller elements running on hardened steel strips.

The path measurement is accomplished by means of induction coils which are placed immediately adjacent to the directional guides and which are thus little influenced by tilting.

For operation requiring little operating personnel it is of essential importance that in addition to securing thermal stability and eliminating process debris one should have automatic surveillance of the tools. Especially exposed to process damage are the slender tools such as thin spiral borers, countersinkers, thread borers, centering borers and the like. Before being used in cutting they can be checked by means of an electronic camera which observes the contour of the tool against an illuminated background and compares it with a target value. In addition to this recognition of severe fractures, a surveillance system assures that tool replacement is accomplished promptly before there is excessive wear. The corresponding signal appears on the pictures screen. A further step toward automatic low-personnel operation is represented by the possibility of measuring and appropriately evaluating by means of a replaceable measurement pickup chucking attitudes, oversizes, position errors, consequences of wear and other deviations from programmed initial states, intermediate states and final states of the workpieces.

For example, there was developed a subprogram for determining and correcting the position of the palettes or of the workpiece relative to the center of rotation of the fourth NC axis as well as to determine the angular rotational error of the latter with reference to the translatory machine coordinate system. By means of a double probing, taking place at a specific interval, over a reference area lying in the Z direction the obliquity of position is determined and thereupon within the guidance system the requisite rotational correction angle of the A axis is calculated and executed (Figure 7).

The determination of the displacement which manifests itself as an eccentricity relative to the center of rotation of the axis is accomplished by lateral probing of the test piece (left and right), a subsequent 180° rotation and a repeated probing of one lateral surface whose position has been changed by the rotation.

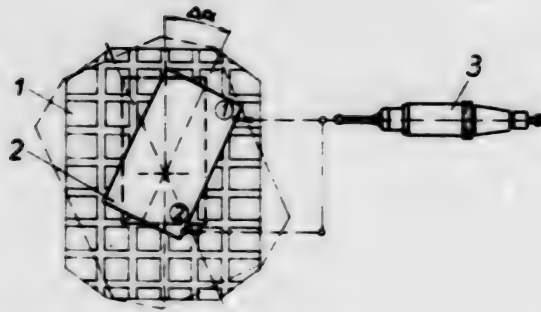


Figure 7. Position determination and position correction of obliquely chucked workpieces by means of measuring probes: 1--palette; 2--workpieces; 3--measuring probes; ①, ②--probe points in sequence; $\Delta\alpha$ --amount of correction (rotational).

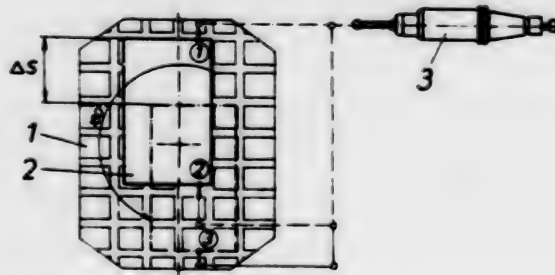


Figure 8. Position determination and position correction by means of measuring probes of workpieces chucked in a position which is displaced relative to the center of rotation: 1--palette; 2--workpieces; 3--measuring probes; ①, ②, ③--probe points in sequence; ΔS --amount of correction (translatory).

By means of these three measurement points the eccentric position is determined and stored and is taken into account automatically in processing two sides (Figure 8).

Naturally, it is possible in this way to make measurements only with that degree of accuracy which is permitted by the no-load accuracy of the machine and by the error of the measuring probe. Since, however, the positioning accuracy lies within a 10- μm range, the rechucking accuracy within 5 μm and the probing accuracy likewise lies within 5 μm it is thus possible to carry out a series of measurement operations with satisfactory results. In this way arbitrary measurement operations may be interpolated into the work cycle. At specifically limited time intervals, for example, it is possible to determine the thermal drift of the zero point of the workpiece position relative to the guidance coordinate system and it is possible for this to be corrected so that the stability of the workpiece quality can be guaranteed while maintaining a low level of human supervision. In a similar way dimensional deviations, excessive dimensions or chucking errors may be determined and corrected without the intervention of an operator.



Figure 9. Computer-guidance CNC 6000 (Numerik "Karl Marx," Karl-Marx City/GDR).

Guidance Using Specific Software Adaptation

For the new type of flexible manufacturing cell the guidance system CNC 6000 (Figure 9) is employed which in particular permits a specific adaptation of the software to the existing possibilities. The system permits path processings by 2D-circular, 2.5D-helical and 3D-straight line interpolation. Further characteristic features are:

- i. convenient operation via an alphanumeric keyboard and picture screen display in conjunction with extensive editing possibilities and the output of an optimized program by means of an attachable punched tape perforator;
- ii. extremely simple programmability in conjunction with an extensive subprogram technique involving 99 possible programs, capable of fourfold subnesting, containing in addition to frequently recurring process-specific processing cycles and machine-specific cycles (such as tool and workpiece changing) a series of geometric computing programs for the determination and fixing of the

workpiece contour. Equidistant correction makes possible in principle the workpiece contour programming as well as the dimension programming in circular milling and axis reflection;

iii. correction possibilities for measurement system errors (9' per axis) and reversal chucking (3 values per axis).

The guidance system processes the analogous signal inputs of the thermal sensors of the surveillance system of the supporting carriage, of the work spindles, of the workspace of the tools and of the stationary times. It carries out continuous self-diagnosis and reports any occurring troubles through error displays on the picture screen.

The measurement points recorded by the measuring probe and telemetrically transferred to the guidance system are processed via subprograms into diagnoses of the workpiece attitude and of the working accuracy.

Usefulness of the Facility Can Be Extremely High

In the test runs turning moments of 500 Nm were applied using knife-head milling tools of steel having a tensile strength of 500 N/mm². In such a case it was possible to mill with a cutting depth of 10 mm, a cutting breadth of 130 mm and a tool advance rate of 200 mm/min a cutting volume of 260 cm³/min.

From the optimized adaptation of the guidance to the machine it was possible to extract considerable reserves of productivity. An example of this is the automatic tool advance calculation as a function of dimension in the milling of outside corners. While in the case of guidance systems of the older generation the corner, as shown on the left side of Figure 10, was produced by cutting straight path segments, in this design the corner is not milled simply by moving over a quarter circle but is produced at a higher optimal tool advance velocity corresponding to the size of the material to be removed (Figure 10, right). By this procedure alone it was possible to reduce the processing time for the sample workpiece by 12 percent.

Further substantial increases in productivity result from minimization of the auxiliary time. Features contributing especially to this are:

- i. the free fall of the metal shavings from the cutting site into the automatic transport facility supported by the intensive programmable process lubrication and process cooling which take place in two pressure stages;
- ii. the automatic in-process measurement technique which triggers immediately required corrections or displays them;
- iii. the convenient operation including possibilities for program optimization with image screen support made possible by means of the new CNC 6000;
- iv. the thermal control and diagnostics for stable maintenance of precision;
- v. the possibilities for self-diagnosis in the guidance system.

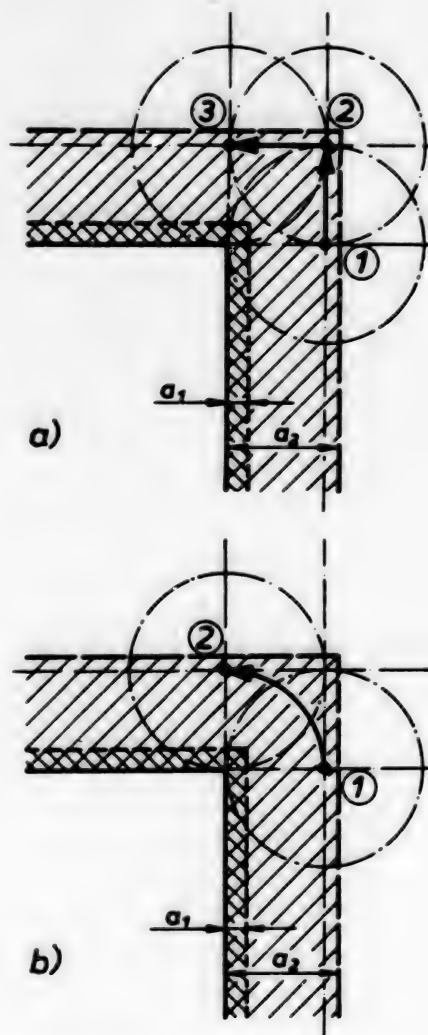


Figure 10. The use of path guidance in milling right-angled or oblique-angled cornerpoints: on the left--the original state (path guidance); on the right--the new state (with corner augmentation of forward advance); ①, ②, ③--point sequence of the tool path; a_1 , a_2 --milling breadths.

It is expected that as a result of the total of all these measures it will be possible to achieve an annual time saving in productive readiness amounting to at least 400 hours.

8008
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RAPID DEVELOPMENT OF MICROELECTRONICS INDUSTRY DEFENDED

Budapest HETI VILAGGAZDASAG in Hungarian No 31, 31 Jul 82 pp 50-51

[Interview with Bence Adorjan, CSc, retired deputy director of the National Technical Development Commission's Institute for the Coordination of Computer Technology, by HETI VILAGGAZDASAG reporter Gizella Tarnoi]

[Text] The world regarded as a sensation a report entitled "Microelectronics and Society--A Matter of Life and Death" and prepared by the Club of Rome that comprises about 100 scientists of world renown. The study was reviewed as a series in HETI VILAGGAZDASAG. Parallel with this study there appeared in the spring of this year a Hungarian analysis of the social impacts of the development of microelectronics, which raises the same issues and arrives at more or less the same conclusions as the scientists of the Club of Rome. The author of "A Szamitastechnika Valaszuton" (Computer Technology at the Crossroads) is Bence Adorjan, age 61, a science candidate, retired deputy director of the OMFB [National Technical Development Commission] Institute for the Coordination of Computer Technology (Szamitastechnikai Koordinacios Intezet). We interviewed the author about his book.

HETI VILAGGAZDASAG: In the Hungarian economy the microelectronics industry is not dictating a dangerous speed, and therefore its social impacts are not frightening for the time being. Why are you nevertheless so concerned with this problem that you have systematized your thoughts in book form?

Adorjan: I think it is very important to assess everything possible in advance, so that we will not be unprepared and will have time to consider what our most sensible course of action will be in the future. Although very many gifted persons are being born in Hungary, we are not utilizing adequately the possibilities inherent in the human intellect. Yet we have long been aware that we are not a country of iron and steel and must therefore seek the key to our success in our intellectual resources, not in our natural conditions. We must assess in advance what fields will border on microelectronics and encourage the training of specialists, or actually train them, accordingly. We must make computers, or at least calculators, available to as many children as possible, so that the computer literacy of the younger generation may increase in these contiguous fields.

HETI VILAGGAZDASAG: A blessing or curse, evolution or revolution, life or death--these are the questions asked by the scientists of the Club of Rome. In your opinion, are these questions timely also for us, and do they arise in the same manner as in Western countries?

Adorjan: They are indeed very timely in my opinion, but with the opposite sign. While the developed capitalist countries fear that the development of microelectronics will further increase the army of the unemployed and that the best workers in occupations that are still well-established today will find themselves on the street, we fear that we will not succeed in making every competent official duly aware that it would be a mortal sin to neglect the development of microelectronics. It is obvious that in every field, ranging from medical instruments through computers to the production of motor vehicles, we can be successful only if we rapidly apply the latest achievements in science and technology.

HETI VILAGGAZDASAG: In the richer capitalist countries microelectronics has penetrated not only material production but numerous areas of everyday life as well. Where can a Hungarian encounter this all-transforming technology in his everyday life?

Adorjan: Everywhere, if he goes about with open eyes. Microelectronics today plays an important role not only in production; it is penetrating increasingly into nonproductive services and even into households. Consider the latest programmable washing machines, or an integrated-circuit television set. These are the most simple examples, and even more complicated ones are within attainable reach. Imagine what the social impact will be if the television-based Teletext or Viewdata system spreads. With the help of his already existing telephone and television set, plus a minimum of additional hardware, a subscriber will be able to use in his own home the most diverse computer services. This will not only include entertainment and information services, but will also permit working at home in a variety of jobs. This form of microelectronics application is significant not only because less investment will be required in workplaces and also the time and expense of commuting can be saved, but also because working at home can set an example in family life and in the education of children in particular, and these are already social impacts.

HETI VILAGGAZDASAG: From what you say it appears that you regard all this as available in the immediate future. But to me it sounds utopistic. For example, I do not even have a telephone at home, and not because I have not applied for one.

Adorjan: Well, yes. Today a telephone is still a problem in many families. But the subscriber who has both a telephone and a television set will sooner or later be able to contact, at minimal additional cost, a central data bank of the kind that is being tested experimentally also in Hungary. I could go on listing examples of the applications in the developed countries where the Teletext or Viewdata system has already been introduced, and other future applications of such systems are perhaps unlimited. But one thing is certain: one of the most important results of the process of the development of electronics will be the same in Hungary as the one already perceptible in the industrially developed capitalist countries. What I have in mind is that people will have to become accustomed to the fact that they will have to change their occupa-

tions during their lifetime, perhaps even more than once, and that they will have to study continuously. The era of our grandfathers, when an occupation passed on from father to son, is long past. Through the applications of microelectronics, every customary machine and technology could change practically overnight.

HETI VILAGGAZDASAG: I read in a study that at least 40 percent of all office work can be automated. This figure alone indicates that millions could be forced to quit their jobs, as a result of which their present way of life could change. How can a society survive such a profound transformation?

Adorjan: I think it is very essential that computerization and electronics applications proceed in accordance with a state policy, for the very reason that reminded you of this example first of all. In my opinion, electronics should be introduced primarily where man has to work in an environment that is dangerous or injurious to health, and where raw materials and energy can be saved. Today we already have manpower shortages in many areas. To remain with the examples cited in your question, I do not believe that the surplus manpower replaced by the automation of office work will flow to occupations in which there are manpower shortages. To cite merely one example: the shortage of freight handlers at railroad freight yards is an enormous problem. But how many of the former office workers replaced by mechanization would be willing to load freight at railroad freight yards? In my opinion, not one. However, there are many branches of production--for example, the production of medical instruments or the engineering industry--where computerization would be of basic importance. If in these areas we could quickly apply the advances in microelectronics, we would also be able to alleviate our economic problems. However, this presupposes that we use electronics not because it is fashionable, but to satisfy actual needs.

HETI VILAGGAZDASAG: There has been mention of Hungarian microelectronics only recently. Mostly since December of 1981, when the Council of Ministers approved the electronic components program, allocated 4.5 billion forints for its realization, and decided to establish a Microelectronics Enterprise (Mikroelektronikai Vallalat). Is this sum sufficient?

Adorjan: I believe that spending on electronics is not keeping pace even with the already modest growth of national income. Stated differently: although national income is not growing as fast as previously, spending on electronics is not keeping pace even with this slower growth rate. Yet the widescale application of electronics could "pull up" the other branches of industry. The installed electronics equipment could make our machine tools and instruments more valuable, but they could also increase our results in agriculture, transport and education.

HETI VILAGGAZDASAG: The governments of the developed capitalist countries are supporting microelectronics with billions of dollars. But perhaps we do not even have to go West to obtain data for comparisons. Czechoslovakia, Bulgaria and the GDR are each spending the equivalent of 40 to 60 billion forints for the development of microelectronics. If we compare to this our 4.5 billion forint allocation, it is hard to believe that we will be able to overcome our lag within the foreseeable future.

Adorjan: Originally more was to have been earmarked for this program than the amount actually approved. The base shrank because the national economy's ability to finance such programs has diminished in recent years. For this very reason the available amount will have to be spent that much more prudently, and we must also try to have it increased if possible.

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BRIEFS

URANIUM MINERALS DISCOVERY--In the Nowa Ruda region, a small increase in the uranium content of the Glinik bed floor has been recorded; on the other hand, the main uranium-bearing horizon is found in the middle part of the Glinik beds in contrast to the Grzmiaca region and the area situated northwest of it, in which the uranium mineralization points occur in the roof of the Glinik beds. In the Stephanian, the uranium mineralization points occur in various parts of the Ludwikowice beds. Uranium minerals in the Glinik and Ludwikowice beds in Nowa Ruda are indicated by uranium oxides--uranium black--and secondary uranium minerals from the sulphate group--zippeite and uranopilite. Mineral paragenesis--uranium black, pyrite, chalcopryrite, sphalerite and galena--in mineralized uranium-bearing horizons of the Glinik beds in the Nowa Ruda region indicates an analogy with the uranium-bearing formations in the Grzmiaca region. [Excerpt] [Warsaw KWARTALNIK GEOLOGICZNY in Polish No 2, Apr-Jun 82 pp 287-292]

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